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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,125	03/28/2001	Etsuya Matsutani	2556USOP	7053

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,125	MATSUTANI ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2004 and 01 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040908*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed September 8, 2004 is acknowledged and has been entered. Claims 1-11 have been canceled. Claims 13-20 have been added.

2. The amendment filed March 1, 2005 is acknowledged and has been entered. Claims 12, 13, 16, and 17 have been amended.

3. Claims 12-20 are pending in the application and are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The following Office action contains NEW GROUNDS of objection or rejection necessitated by amendment.

Information Disclosure Statement

6. The information disclosure filed September 8, 2004 has been considered. An initialed copy is enclosed.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, Applicant's amendments and/or arguments submitted September 8, 2004 and March 1, 2005 have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed June 9, 2004.

Grounds of Rejection Maintained

8. The rejection of claims 12-14 and 16-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

This is a "written description" rejection.

The ground of this rejection is set forth in section 9 of the preceding Office action mailed June 9, 2004.

At page 6 of the amendment filed September 8, 2004, Applicant has asserted that this ground of rejection is moot in light of the amendment.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 12-15 and 16-20 are directed to a genus of "tyrosine kinase inhibitors of a cell growth factor receptor possessing tyrosine kinase activity".

As explained in the preceding Office action, PD153035 cannot be reasonably be regarded as representative of the genus of such agents because the members of the genus vary markedly in both structure and function. Moreover, the specification fails to disclose a particularly identifying (i.e., substantial) structural feature that is common to at least a substantial number of members of the genus, which correlates with the common ability of the members to inhibit the activity of a cell growth factor receptor possessing tyrosine kinase activity.

As also explained in the preceding Office action, the claims are directed to such tyrosine kinase inhibitors that inhibit the activity of a member of a genus of "cell growth factor receptors possessing tyrosine kinase activity". The members of the genus of substances possessing substantially the same activity as EGF, or any other cell growth factor or receptor thereof, cannot be regarded as adequately described, since, here again, the members of the genus are structurally and functionally disparate.

Given these facts, it is apparent that the supporting disclosure fails to provide an adequate written description of the claimed invention, since it would not permit the skilled artisan to

immediately recognize, envision, or distinguish at least a substantial number of the members of the genus of "tyrosine kinase inhibitors of a cell growth factor receptor possessing tyrosine kinase activity", which are needed to use the claimed invention and therefore would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

9. Claims 12-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a composition for repressing proliferation of hormone-dependent prostate cancer, said composition comprising the peptide of SEQ ID NO: 1, or a salt thereof, wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5, and the tyrosine kinase inhibitor PD153035, **does not reasonably provide enablement for making and using** a composition for suppressing the metastasis or recurrence of a cancer by retarding the transformation of a hormone-dependent cancer to a non-hormone dependent cancer or for preventing cancer, including prostatic cancer, ovarian cancer, cervical cancer, and breast cancer, wherein said composition comprises the peptide of SEQ ID NO: 1, or a salt thereof, wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5, and any tyrosine kinase inhibitor of a cell growth factor receptor possessing tyrosine kinase activity, including the tyrosine kinase inhibitor PD153035. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The ground of this rejection is set forth in section 10 of the preceding Office action mailed June 9, 2004.

At page 6 of the amendment filed September 8, 2004, Applicant has asserted that this ground of rejection is moot in light of the amendment.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

The factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working

examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to make and use the invention as claimed.

Upon careful consideration of these factors, a preponderance of factual evidence of record indicates that the amount of guidance, direction, and exemplification contained in the supporting disclosure would not be sufficient to enable the skilled artisan to use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

10. The rejection of claims 12-17 under 35 U.S.C. 102(b) as being anticipated by WO 98/32423 A1 (of record), as evidenced by Schally et al. (of record) and/or Pinski et al. (of record), is maintained.

The ground of this rejection is set forth in section 16 of the preceding Office action mailed June 9, 2004.

At page 7 of the amendment filed September 8, 2004, Applicant has traversed this ground of rejection, arguing that the prior art does not teach the claimed invention.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

At page 10 (paragraph [24]), the specification discloses:

> "To retard the transformation of a hormone-dependent cancer to a non-hormone-dependent cancer (transformation is retarded)" means that in applying hormone therapy to a hormone-dependent cancer described above, the transformation of a hormone-dependent cancer to a non-hormone-dependent cancer is retarded by suppressing or retarding the proliferation of a cancer that has become unresponsive to hormone therapy as a result of a long-term administration of a hormonal agent (non-hormone-dependent cancer).

Accordingly, the claimed compositions and methods for retarding the transformation of a hormone-dependent cancer to a hormone-dependent cancer are interpreted as claims to composition and methods for suppressing or retarding proliferation of a cancer, such that its progression to a non-hormone-dependent state is suppressed or retarded.

As evidenced by Schally et al., somatostatin derivatives, such as those disclosed by WO 98/32423 A1 at, e.g., page 10, line 35, through page 11, line 11, are agents that inhibit the activity of EGF or its receptor.

As evidenced by Pinski et al., bombesin peptide, such as that disclosed by WO 98/32423 A1 at, e.g., page 11, line 25, is an agents that inhibits the activity of EGF or its receptor.

WO 98/32423 A1 teaches a the production and use of a composition of the peptide of SEQ ID NO: 1, or a salt thereof (particularly, acetate), wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5; see entire document, particularly page 13, lines 27-36. WO 98/32423 A1 teaches the peptide is an LH-RH agonist; and moreover, the prior art teaches a composition of the LH-RH agonist and either a somatostatin derivative or bombesin, or both, can be used to treat diseases dependent on LH-RH or hormones induced thereby, including prostate cancer, cervical cancer, ovarian cancer or breast cancer; see, e.g., the abstract; page 8, lines 13-16; page 10, line 32, through page 12, line 9; page 13, lines 27-36; page 37, lines 26, through page 38, page 17; and claim 56.

Claim Rejections - 35 USC § 103

11. The rejection of claims 12-17 under 35 U.S.C. 103(a) as being unpatentable over Schally et al. (of record), or Pinski et al. (of record), or U.S. Patent No. 6,211,215 B1, in view of WO 98/32423 A1, is maintained.

The ground of this rejection is set forth in section 19 of the preceding Office action mailed June 9, 2004.

At pages 7 and 8 of the amendment filed September 8, 2004, Applicant has traversed this ground of rejection, arguing that the prior art does not teach or suggest the increase in expression of growth factor receptor by the treatment with LH-RH analog therapy.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

WO 98/32423 A1, Schally et al., Pinski et al., and U.S. Patent No. 6,211,215 B1 ('215) teach that which is set forth above and/or in any of sections 14-19 of the preceding Office action. Although none of Schally et al., Pinski et al., and '215 teach or suggest an LH-RH agonist, which is the peptide of SEQ ID NO: 1, or a salt (acetate) thereof, wherein the sixth amino acid residue

is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5, in further view of the teachings of WO 98/32423 A1, it would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a composition comprising an inhibitor of tyrosine kinase activity, as taught by '215, and the peptide of SEQ ID NO: 1, or a salt thereof, and particularly the acetate thereof, wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5, according to WO 98/32423 A1, because each of none of Schally et al., Pinski et al., and '215 suggest the combination of the inhibitor of tyrosine kinase activity and an LH-RH agonist can be used more effectively treat prostate cancer. One of ordinary skill in the art would have been motivated to do so to treat prostate cancer.

In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., the increase in expression of growth factor receptor by the treatment with LH-RH analog therapy) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Double Patenting

12. The rejection of claims 12-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-30 of U.S. Patent No. 6,716,863 B2 is maintained.

The ground of this rejection is set forth in section 21 of the preceding Office action mailed June 9, 2004.

At page 8 of the amendment filed September 8, 2004, Applicant has traversed this ground of rejection, arguing that the compound of the present invention is not specifically disclosed in the prior patent and furthermore, the prior claims do not teach or suggest that transformation of a hormone-dependent cancer to a non-hormone dependent cancer can be suppressed by administering the compound in combination with a tyrosine kinase inhibitor.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and issued claims are drawn to nearly the same compositions comprising an LH-RH agonist and an agent that inhibits the action of EGF and its receptor, or nearly the same methods for producing the composition or using the composition to treat cancer.

In response to Applicant's argument that the prior patent does not teach an LH-RH agonist, which is the peptide of SEQ ID NO: 1, or a salt (acetate) thereof, wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C2H5, as noted in the preceding Office action, claim 30 of the patent recites the LH-RH antagonist is "leuprorelin or a salt thereof". An acetate salt of leuprorelin is "leuprolide", which is a generic drug sold under a variety of different tradenames, e.g., **ELIGARD®** leuprolide acetate is a peptide having the structure recited in claim 12-17 of the instant application.

In response to Applicant's argument that the prior claims do not teach or suggest that transformation of a hormone-dependent cancer to a non-hormone dependent cancer can be suppressed by administering the compound in combination with a tyrosine kinase inhibitor, the prior claims teach or suggest administering the combination to the same population, namely mammals affected by cancer. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Wiseman,* 201 USPQ 658 (CCPA 1979). Furthermore, granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. See *In re Baxter Travenol Labs,* 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP § 2145. The Court of Appeals for the Federal Circuit has stated that "[I]t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable" See *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1575, 1936 (Fed. Cir. 1990) (emphasis in original). See also *Bristol-Myers Squibb Company v. Ben Venue Laboratories*, 58 USPQ2d 1508 (CAFC 2001) at 1514: "Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent". As to inherency, the Court has noted that "[u]nder the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." *Mehl/Biophile Int'l Corp. v. Miligraum*, 192 F.2d 1362,

1366, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999) (citations omitted). Moreover, "[w]here [...] the result is necessary consequence of what was deliberately intended, it is no import that the article's authors did not appreciate the results." *Mehl/Biophile Int'l Corp*, 192 F.2d 1362, 52 USPQ2d at 1307. See also: *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993); and MPEP §§ 2112 [R-2] and 2112.02 [R-2].

13. As explained in section 22 of the preceding Office action, Applicant is reminded that the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 6,716,863 B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

14. The provisional rejection of claims 12-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-39 of copending Application No. 10/620,706 is maintained.

The ground of this rejection is set forth in section 23 of the preceding Office action mailed June 9, 2004.

At page 8 of the amendment filed September 8, 2004, Applicant has argued that this ground of rejection was rendered moot by the amendment.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in section 23 of the preceding Office action.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. As addressed in section 24 of the preceding Office action, in order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

New Ground of Objection

16. Claims 12-20 are objected to as being drawn in the alternative to a species of invention that does not share the same special technical feature of the elected species of invention.

Claims 12-20 are drawn in the alternative to a method comprising administering cyproterone, rather than the peptide of SEQ ID NO: 1, or a salt thereof, wherein the sixth amino acid residue is D-leucine and the ninth amino acid residue is proline-NH-C_2H_5. Although both species of invention appear to be related, since both cyproterone and the peptide are described in the claims as "hormonal agents", as evidenced by the outstanding rejections under 35 U.S.C. §§ 102 and 103, the technical feature that appears to link the inventive concepts does not constitute a special technical feature as defined by PCT Rule 13.1, as it does not define a contribution over the prior art. Therefore, the special technical feature of each species of invention to which the claims are drawn are different; the special technical feature of the elected species of invention is administering the peptide, whereas the special technical feature of the non-elected species of invention is administering cyproterone.

Appropriate correction is required.

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
May 25, 2005